

## Studies of the ADP-ribose Pyrophosphohydrolase Complexes

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Abstract No. gabe4213

Beamline(s): **X8C, X25**

Nudix hydrolases, previously known as MutT proteins catalyze the hydrolysis of diverse nucleoside diphosphates. The family is characterized by the consensus sequence GX<sub>5</sub>EXREAXEEX<sub>2</sub>L. This sequence appears to be a versatile nucleoside binding and catalytic site present in more than two hundred enzymes found throughout nature, from archae and prokaryotes to eukaryotes. The common feature of the substrates of Nudix enzymes is the diphosphate linkage that is hydrolyzed by the enzymes. The ADP-ribose pyrophosphatase, a member of this family, catalyses the hydrolysis of ADPR into AMP and P-ribose.

Data of the selenomethionine replaced ADP-ribose pyrophosphatase with and without metal were collected on beamlines X25 and X8C. We have determined the crystal structure of the monoclinic crystal form of the apo seleno methionine replaced-ADP ribose pyrophosphatase. Crystals were grown by vapor diffusion at 18C using polyethylene glycol as precipitant. The structure was determined by molecular replacement using the model of the orthorhombic crystal form using the program AMORE. The initial model of the dimer was refined using CNS. The model of the data collected from ADP-ribose pyrophosphate crystals soaked with Mg<sup>+2</sup> is being refined.

The crystals were monoclinic, P21, cell dimensions a=53.34Å, b=65.54Å, c=69.29Å, β=108.47°. The Matthews coefficient for observed atoms is V<sub>m</sub>=2.86 with a unit cell volume of 261608. Before we have shown that amino acids from both monomers contribute to each active site and how the conserved primary sequence relates to specificity of the family. The new Mg/ADPR-ase structure would confirm the site of the metal binding site and the identity of the amino acids involve in the coordination of the metal.

Bessman, M.J., Frick, D.N., O'Handley, S.F. The MutT Proteins or "Nudix"Hydrolases, a family of versatile, widely distributed, housecleaning enzymes. JBC, 271:25059-25062, 1996.

Gabelli, S.B. The versatility of the Nudix hydrolases as revealed by the ADP-ribose pyrophosphatase. PhD thesis, Baltimore, MD. 2000.